

NMCP COVID-19 Literature Report #70: Friday, 18 June 2021

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Purpose: These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

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The Big Picture

News in Brief

"The CDC's No. 2 official says the U.S. isn't ready for another pandemic" ([NPR](#)).

"Some pandemic health habits deserve to stay: We need a public health culture change informed by lessons from COVID" ([Sci Am](#)).

Long Reads

"The fundamental question of the pandemic is shifting: We understand how this will end. But who bears the risk that remains?" ([Atlantic](#)).

"The forever virus: A strategy for the long fight against COVID-19" ([Foreign Affairs](#)).

"The COVID lab-leak hypothesis: what scientists do and don't know—*Nature* examines arguments that the coronavirus SARS-CoV-2 escaped from a lab in China, and the science behind them" ([Nature](#)).

"How the COVID pandemic is changing global science collaborations: The pandemic and political tensions might slow the march towards more globalized science" ([Nature](#)).

"How the world ran out of everything: Global shortages of many goods reflect the disruption of the pandemic combined with decades of companies limiting their inventories" ([NYT](#)).

Special Reports and Other Resources

CGD: [A Path to Resiliency: Mitigating the Impacts of COVID-19 on Essential Medicines Supply Chains \[pdf\]](#) (June 2021)

"COVID-19 has put a spotlight on health product supply chains, highlighting the challenges in multiple steps in the global supply chain. This paper seeks to understand the impact of COVID-19 on the supply chain of a subset of essential medicines. It identifies the main categories of blockages in the global supply chain created by COVID-19, then uses data on trade flows, wholesalers, and pharma companies, and from surveys, to track the impact.

There was significant short-term disruption to manufacturing caused by COVID-19. Surveys, pharmacy, and export data indicate that COVID-related disruptions impacted the supply of essential medicines, but this varied greatly by markets and product.

The paper highlights that (1) data-driven approaches should be considered to make supply chains more robust, (2) solutions must account for the political and institutional landscape,

(3) price surges benefit the wealthiest, and (4) local solutions are often needed to manage global shocks.

More research is needed, particularly into how to obtain granular data to track supply shocks in real time? How do we increase surge capacity? Is it possible to improve procurement practices through pooled procurement, where applicable? And can pharmaceutical production be diversified, with products produced regionally to limit the risk of disruption?"

SARS-CoV-2 Virus and Variants

News in Brief

The Delta variant, first identified in India, now accounts for 10% of US cases of COVID-19, according to CDC data ([CIDRAP](#): see also: [CDC COVID data tracker](#)).

"More transmissible, wilier variant makes Covid-19 vaccinations even more crucial, experts say" ([STAT](#)).

"Has a 'Moscow strain' of coronavirus emerged?" ([Moscow Times](#))

"How a rampant coronavirus variant blunts our immune defences[sic]: The rapid spread of the B.1.1.7 variant — also called Alpha — might be linked to its ability to dampen the body's initial immune response" ([Nature](#)).

Peer-Reviewed Articles

JAMA Pediatr: [Comparison of Symptoms and RNA Levels in Children and Adults With SARS-CoV-2 Infection in the Community Setting](#) (11 June 2021)

"Question How is the presence of symptoms associated with SARS-CoV-2 RNA levels in children vs adults in the community?

Findings In this cross-sectional study of 555 children and adults with SARS-CoV-2 confirmed by reverse transcription–polymerase chain reaction, symptomatic individuals had higher SARS-CoV-2 RNA levels (as indicated by lower mean cycle threshold values) compared with asymptomatic individuals. No significant differences in RNA levels were found between asymptomatic children and asymptomatic adults or between symptomatic children and symptomatic adults.

Meaning Regardless of age, in this community-based study, SARS-CoV-2 RNA levels were higher in symptomatic individuals."

See also: [editorial](#)

MMWR: [Genomic Surveillance for SARS-CoV-2 Variants Circulating in the United States, December 2020–May 2021](#) (11 June 2021)

"What is already known about this topic? SARS-CoV-2 variants have the potential to affect transmission, disease severity, diagnostics, therapeutics, and natural and vaccine-induced immunity.

What is added by this report? CDC's genomic surveillance for SARS-CoV-2 variants generates population-based estimates of the proportions of variants among all SARS-CoV-2 infections in the United States. During April 11–24, 2021, the B.1.1.7 and P.1 variants represented an estimated 66.0% and 5.0% of U.S. infections, respectively, demonstrating the potential for new variants to emerge and become predominant.

What are the implications for public health practice? Robust genomic surveillance can help guide prevention strategies (e.g., enhanced vaccination coverage efforts) and clinical management decisions (e.g., monoclonal antibody distribution) to control the COVID-19 pandemic in the United States."

Clin Infect Dis: [Increased household secondary attacks rates with Variant of Concern SARS-CoV-2 index cases](#) (09 June 2021)

"We compared secondary attack rates in households with B.1.1.7 variant of concern (VOC) versus non-VOC index cases in a matched cohort in Ontario, Canada. The secondary attack rate for VOC index cases was 1.31 times higher than non-VOC index cases. This increase was particularly accentuated for asymptomatic or presymptomatic index cases."

Lancet Respir Med: [Persistence of SARS-CoV-2 RNA in lung tissue after mild COVID-19](#) (09 June 2021)

"To our knowledge, this is the first report of long-term (>100 days) persistence of SARS-CoV-2 RNA in lung tissue of an immunocompetent patient after convalescing from COVID-19. The debris-like tissue that contained SARS-CoV-2 RNA might be composed of degenerated endothelial cells that had detached from vessel walls, dysmorphic syncytial elements of pneumocytes, or dead neutrophilic plugs in the interstitium.

We speculate that this debris-like tissue might shield SARS-CoV-2 RNA from degradation."

Nature: [Immunogenicity of Ad26.COV2.S vaccine against SARS-CoV-2 variants in humans](#) (09 June 2021)

"The Ad26.COV2.S vaccine has demonstrated clinical efficacy against symptomatic COVID-19, including against the B.1.351 variant that is partially resistant to neutralizing antibodies. However, the immunogenicity of this vaccine in humans against SARS-CoV-2 variants of concern remains unclear. Here we report humoral and cellular immune responses from 20 Ad26.COV2.S vaccinated individuals from the COV1001 phase 1/2 clinical trial against the original SARS-CoV-2 strain WA1/2020 as well as against the B.1.1.7, CAL.20C, P.1., and B.1.351 variants of concern. Ad26.COV2.S induced median pseudovirus neutralizing antibody titers that were 5.0- and 3.3-fold lower against the B.1.351 and P.1 variants, respectively, as compared with WA1/2020 on day 71 following vaccination. Median binding antibody titers were 2.9- and 2.7-fold lower against the B.1.351 and P.1 variants, respectively, as compared with WA1/2020. Antibody-dependent cellular phagocytosis, complement deposition, and NK cell activation responses were largely preserved against the B.1.351 variant. CD8 and CD4 T cell responses, including central and effector memory responses, were comparable among the WA1/2020, B.1.1.7, B.1.351, P.1, and CAL.20C variants. These data show that neutralizing antibody responses induced by Ad26.COV2.S were reduced against the B.1.351 and P.1 variants, but functional non-neutralizing antibody responses and T cell responses were largely preserved against SARS-CoV-2 variants. These findings have implications for vaccine protection against SARS-CoV-2 variants of concern."

Sci Transl Med: [Antibodies elicited by mRNA-1273 vaccination bind more broadly to the receptor binding domain than do those from SARS-CoV-2 infection](#) (08 June 2021)

"The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants with mutations in key antibody epitopes has raised concerns that antigenic evolution could erode adaptive immunity elicited by prior infection or vaccination. The susceptibility of immunity to viral evolution is shaped in part by the breadth of epitopes targeted by antibodies elicited by vaccination or natural infection. To investigate how human antibody responses to vaccines are influenced by viral mutations, we used deep mutational scanning to compare the specificity of polyclonal antibodies elicited by either two doses of the mRNA-1273 COVID-19 vaccine or natural infection with SARS-CoV-2. The neutralizing activity of vaccine-elicited antibodies was more targeted to the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein compared to antibodies elicited by natural infection. However, within the RBD, binding of vaccine-elicited antibodies was more broadly distributed across epitopes compared to infection-elicited antibodies. This greater binding breadth means that single RBD mutations have less impact on neutralization by vaccine sera compared to convalescent sera. Therefore, antibody immunity acquired by natural infection or different modes of vaccination may have a differing susceptibility to erosion by SARS-CoV-2 evolution."

Vaccines and Vaccine Hesitancy

News in Brief

"A new type of COVID-19 vaccine could debut soon" ([NPR](#)).

"Does vaccinating adults stop kids from spreading COVID too? Mass vaccination drives in several countries are providing new data on the extent to which adult vaccination protects children — but the conclusions are mixed" ([Nature](#)).

Anti-vaccine activists are using the CDC's Vaccine Adverse Event Reporting System (VAERS) to spread misinformation ([NPR](#)).

The headline says it all really: "China is vaccinating a staggering 20 million people a day—Scientists are impressed by China's juggernaut of a vaccination drive, through which it is currently administering nearly 60% of all COVID-19 vaccine doses globally" ([Nature](#)).

Effectiveness

A CDC study shows that mRNA vaccines confer 91% risk reduction of infection in people who are fully vaccinated ([CDC](#); see also: [medRxiv preprint](#)).

Novavax's COVID vaccine shows 90% efficacy; also of note, the clinical trial was highly diverse with 44% nonwhite participants ([Science](#); see also: [Novavax press release](#)).

"Mixing COVID-19 vaccines appears to boost immune responses" ([Science](#)).

Long Reads

"COVID-19 vaccines work way better than we had ever expected. Scientists are still figuring out why. 'The truth is, we humans sort of lucked out,' one expert said" ([BuzzFeed](#)).

"Six months of COVID vaccines: what 1.7 billion doses have taught scientists—At a pivotal moment in the pandemic, *Nature* explores key questions about the vaccines that countries are racing to deliver while viral variants spread around the globe" ([Nature](#)).

Peer-Reviewed Articles

Effectiveness

Open Forum Infect Dis: [BNT162b2 vaccine effectiveness in preventing asymptomatic infection with SARS-CoV-2 virus: a nationwide historical cohort study](#) (09 June 2021)

"Background: There is strong evidence regarding the efficacy and effectiveness of BNT162b2 vaccine in preventing symptomatic infection with SARS-CoV-2 virus. There is a relative paucity of data regarding effectiveness in prevention of asymptomatic infection.

Methods: In this real-world observational study, we identified a sub-population of individuals in a large health maintenance organization who were repeatedly tested for SARS-CoV-2 infection by PCR. We included these individuals in the study cohort, and compared those who were vaccinated with BNT162b2 mRNA vaccine to the unvaccinated ones. A positive SARS-CoV-2 PCR test result was used as the outcome. Follow-up period was from January 1, 2021 until February 11, 2021.

Findings: 6,286 individuals were included in the cohort. Seven days following the second vaccine dose, a rate of six positive PCR tests per 10,000 person-days was recorded, compared with a rate of 53 positive tests per 10,000 person-days for the unvaccinated group. The estimated vaccine effectiveness against infection with SARS-CoV-2 virus after two vaccine doses was 89% (95% confidence interval 82%-94%). The estimated effectiveness two weeks following the first vaccine dose was 61% (95% confidence interval 49%-71%).

Interpretation: In this study, vaccination with BNT162b2 reduced infection rates among individuals who underwent screening by frequent SARS-CoV-2 PCR testing. Using a cohort of frequently tested individuals reduced the indication bias for the PCR testing, which enabled estimation of infection rates."

JAMA Netw Open: [Assessment of Effectiveness of 1 Dose of BNT162b2 Vaccine for SARS-CoV-2 Infection 13 to 24 Days After Immunization](#) (07 June 2021)

"Question Is 1 dose of the BNT162b2 COVID-19 mRNA vaccine associated with protection against infection with SARS-CoV-2 and symptomatic COVID-19 in real-world settings?

Findings In this comparative effectiveness study of 503 875 individuals who received 1 dose of the BNT162b2 vaccine, the first dose of the vaccine was associated with an approximately 51% reduction in the risk of SARS-CoV-2 infections at 13 to 24 days after immunization compared with 1 to 12 days after vaccination. The first dose was associated with 54% effectiveness against symptomatic COVID-19.

Meaning The results of this study agree with vaccine efficacy as reported in the phase III randomized clinical trial after 1 dose."

Adverse Effects and Events

JAMA: [Sperm Parameters Before and After COVID-19 mRNA Vaccination](#) (17 June 2021)

"In this study of sperm parameters before and after 2 doses of a COVID-19 mRNA vaccine, there were no significant decreases in any sperm parameter among this small cohort of healthy men. Because the vaccines contain mRNA and not the live virus, it is unlikely that the vaccine would affect sperm parameters. While these results showed statistically significant increases in all sperm parameters, the magnitude of change is within normal individual variation and may be influenced by regression to the mean. Additionally, the increase may be due to the increased abstinence time before the second sample. Men with oligospermia did not experience further decline."

Circulation: [Myocarditis after BNT162b2 and mRNA-1273 Vaccination](#) (16 June 2021)

"Here, we describe 8 patients hospitalized with chest pain who were diagnosed with myocarditis by laboratory and cardiac magnetic resonance imaging (MRI) within 2-4 days of receiving either the BNT162b2 or mRNA-1273 vaccine..."

All individuals were otherwise healthy males between the ages of 21 and 56. All but one patient developed symptoms after their second dose. Systemic symptoms began within 24 hours after vaccine administration in 5 out of 8 patients, with chest pain presenting between 48 and 96 hours later. Chest pain was most commonly described as constant, non-positional, and non-pleuritic (only patient 7 reported pericardial pain), consistent with acute myocarditis mainly without pericardial involvement....

In conclusion, providers should be vigilant for myocarditis after COVID-19 mRNA vaccination; further research is required to understand the long-term cardiovascular risks."

BMJ: [Characterising the background incidence rates of adverse events of special interest for covid-19 vaccines in eight countries: multinational network cohort study](#) (14 June 2021)

"Objective To quantify the background incidence rates of 15 prespecified adverse events of special interest (AESIs) associated with covid-19 vaccines.

Design Multinational network cohort study.

Setting Electronic health records and health claims data from eight countries: Australia, France, Germany, Japan, the Netherlands, Spain, the United Kingdom, and the United States, mapped to a common data model.

Participants 126 661 070 people observed for at least 365 days before 1 January 2017, 2018, or 2019 from 13 databases.

Main outcome measures Events of interests were 15 prespecified AESIs (non-haemorrhagic and haemorrhagic stroke, acute myocardial infarction, deep vein thrombosis, pulmonary embolism, anaphylaxis, Bell's palsy, myocarditis or pericarditis, narcolepsy, appendicitis, immune thrombocytopenia, disseminated intravascular coagulation, encephalomyelitis (including acute disseminated encephalomyelitis), Guillain-Barré syndrome, and transverse

myelitis). Incidence rates of AESIs were stratified by age, sex, and database. Rates were pooled across databases using random effects meta-analyses and classified according to the frequency categories of the Council for International Organizations of Medical Sciences.

Results Background rates varied greatly between databases. Deep vein thrombosis ranged from 387 (95% confidence interval 370 to 404) per 100 000 person years in UK CPRD GOLD data to 1443 (1416 to 1470) per 100 000 person years in US IBM MarketScan Multi-State Medicaid data among women aged 65 to 74 years. Some AESIs increased with age. For example, myocardial infarction rates in men increased from 28 (27 to 29) per 100 000 person years among those aged 18-34 years to 1400 (1374 to 1427) per 100 000 person years in those older than 85 years in US Optum electronic health record data. Other AESIs were more common in young people. For example, rates of anaphylaxis among boys and men were 78 (75 to 80) per 100 000 person years in those aged 6-17 years and 8 (6 to 10) per 100 000 person years in those older than 85 years in Optum electronic health record data. Meta-analytic estimates of AESI rates were classified according to age and sex.

Conclusion This study found large variations in the observed rates of AESIs by age group and sex, showing the need for stratification or standardisation before using background rates for safety surveillance. Considerable population level heterogeneity in AESI rates was found between databases."

Nat Med: [First-dose ChAdOx1 and BNT162b2 COVID-19 vaccines and thrombocytopenic, thromboembolic and hemorrhagic events in Scotland](#) (09 June 2021)

"Reports of ChAdOx1 vaccine-associated thrombocytopenia and vascular adverse events have led to some countries restricting its use. Using a national prospective cohort, we estimated associations between exposure to first-dose ChAdOx1 or BNT162b2 vaccination and hematological and vascular adverse events using a nested incident-matched case-control study and a confirmatory self-controlled case series (SCCS) analysis. An association was found between ChAdOx1 vaccination and idiopathic thrombocytopenic purpura (ITP) (0-27 d after vaccination; adjusted rate ratio (aRR) = 5.77, 95% confidence interval (CI), 2.41-13.83), with an estimated incidence of 1.13 (0.62-1.63) cases per 100,000 doses. An SCCS analysis confirmed that this was unlikely due to bias (RR = 1.98 (1.29-3.02)). There was also an increased risk for arterial thromboembolic events (aRR = 1.22, 1.12-1.34) 0-27 d after vaccination, with an SCCS RR of 0.97 (0.93-1.02). For hemorrhagic events 0-27 d after vaccination, the aRR was 1.48 (1.12-1.96), with an SCCS RR of 0.95 (0.82-1.11). A first dose of ChAdOx1 was found to be associated with small increased risks of ITP, with suggestive evidence of an increased risk of arterial thromboembolic and hemorrhagic events. The attenuation of effect found in the SCCS analysis means that there is the potential for overestimation of the reported results, which might indicate the presence of some residual confounding or confounding by indication. Public health authorities should inform their jurisdictions of these relatively small increased risks associated with ChAdOx1. No positive

associations were seen between BNT162b2 and thrombocytopenic, thromboembolic and hemorrhagic events."

NEJM: [Delayed Large Local Reactions to mRNA Covid-19 Vaccines in Blacks, Indigenous Persons, and People of Color](#) (09 June 2021)

"Delayed large local reactions may be less commonly recognized or reported in BIPOC [Black, Indigenous, or People of Color] vaccine recipients than in White recipients. Such reactions may result in vaccine hesitancy or incomplete vaccination; as such, proactive outreach is needed to increase education regarding these reactions across diverse communities. We hope that this letter encourages additional research and communication regarding cutaneous vaccine reactions, including delayed large local reactions, in BIPOC recipients."

Clin Infect Dis: [Incidence and Characteristics of Delayed Injection Site Reaction to the mRNA-1273 SARS-CoV2 Vaccine \(Moderna\) in a Cohort of Hospital Employees](#) (04 June 2021)

"Background COVID-19 vaccines, primarily mRNA types, are administered to 2,000,000 individuals per day in the US under FDA emergency use authorization.

Methods Observational cohort study of hospital workers who received their first SARS-CoV2 mRNA vaccination between December 14, 2020 and January 8, 2021, including cases reporting onset of an injection site reaction > 48 hours after administration of their first or second dose to an employee hotline.

Results Thirteen female employees, who received mRNA-1273 SARS-CoV2 vaccine (Moderna) during the first three weeks of SARS-CoV2 vaccine rollout at San Francisco General Hospital, reported a pruritic rash at the injection site appearing 3-9 days after receiving their initial dose. Five had milder or similar reactions with earlier onset after the second dose. One additional female employee reported this delayed reaction only after the second dose. None of these 14 employees reported serious adverse events, such as anaphylaxis, or had symptoms severe enough to seek medical attention. These cases represented 1.1% of the 1,275 female employees who received their first mRNA-1273 dose, and 2.0% of the 557 who were 31-45 years old, during this initial vaccine rollout. None of 675 males initiating mRNA-1273 or 3,612 employees of either sex initiating BNT162b (Pfizer) vaccination during this period reported this delayed onset reaction.

Conclusions These results suggest that delayed-onset, injection-site pruritic rashes after mRNA-1273 SARS-CoV2 vaccine administration, lasting up to a week, occur commonly in females, do not lead to serious sequela, and should not deter receipt of the second vaccine dose."

Impact

MMWR: [Decreases in COVID-19 Cases, Emergency Department Visits, Hospital Admissions, and Deaths Among Older Adults Following the Introduction of COVID-19 Vaccine — United States, September 6, 2020–May 1, 2021](#) (11 June 2021)

"What is already known about this topic? COVID-19 vaccination began in the United States in December 2020, and adults aged ≥ 65 years were prioritized in early phases.

What is added by this report? By May 1, 2021, 82%, 63%, and 42% of adults aged ≥ 65 , 50–64, and 18–49 years, respectively, had received ≥ 1 vaccine dose. From November 29–December 12, 2020 to April 18–May 1, 2021, the rate ratios of COVID-19 incidence, emergency department visits, hospital admissions, and deaths among adults aged ≥ 65 years (≥ 70 years for hospitalizations) to adults aged 18–49 years declined 40%, 59%, 65%, and 66%, respectively.

What are the implications for public health practice? The greater decline in COVID-19 morbidity and mortality in older adults, the age group with the highest vaccination rates, demonstrates the potential impact of increasing population-level vaccination coverage."

Vaccine Hesitancy

Psychol Med: [Injection fears and COVID-19 vaccine hesitancy](#) (11 June 2021)

"Background: When vaccination depends on injection, it is plausible that the blood-injection-injury cluster of fears may contribute to hesitancy. Our primary aim was to estimate in the UK adult population the proportion of COVID-19 vaccine hesitancy explained by blood-injection-injury fears.

Methods: 15,014 UK adults, quota sampled to match the population for age, gender, ethnicity, income, and region, took part (19th January–5th February 2021) in an non-probability online survey. The Oxford COVID-19 Vaccine Hesitancy Scale assessed intent to be vaccinated. Two scales (Specific Phobia Scale-blood-injection-injury phobia; Medical Fear Survey–injections and blood subscale) assessed blood-injection-injury fears. Four items from these scales were used to create a factor score specifically for injection fears.

Results: 3927(26.2%) screened positive for blood-injection-injury phobia. Individuals screening positive (22.0%) were more likely to report COVID-19 vaccine hesitancy than individuals screening negative (11.5%), odds ratio=2.18, CI: 1.97-2.40, $p < .001$. The population attributable fraction indicated that if blood-injection-injury phobia were absent then this may prevent 11.5% of all instances of vaccine hesitancy, AF=0.11; 95% CI: 0.09-0.14, $p < 0.001$. COVID-19 vaccine hesitancy was associated with higher scores on the Specific Phobia Scale, $r=0.22$, $p < .001$, Medical Fear Survey, $r=0.23$, $p < .001$, and injection fears,

r=0.25, p<.001. Injection fears were higher in youth and in Black and Asian ethnic groups, and explained a small degree of why vaccine hesitancy is higher in these groups.

Conclusions: Across the adult population, blood-injection-injury fears may explain approximately 10% of cases of COVID-19 vaccine hesitancy. Addressing such fears will likely improve the effectiveness of vaccination programmes."

Treatments and Management

News in Brief

Preliminary data from the RECOVERY Trial suggest that an antibody combination reduces death in seronegative patients with severe COVID-19 ([CIDRAP](#); see also: [medRxiv preprint](#)).

Data from the same trial suggest that aspirin does not improve survival, however ([RECOVERY](#); see also: [medRxiv preprint](#)).

Research

The US government has developed a \$3.2 billion plan to develop and stockpile antivirals to treat COVID and future viral threats ([WP](#)).

"Centivax partners with U.S. Naval Medical Research Center to develop broad-spectrum COVID-19 therapeutic" ([HPN](#)).

Long Reads

"A white-knuckle ride of open COVID drug discovery—In early 2020, a spontaneous global collaboration came together to design a new, urgent antiviral treatment. There are lessons in what happened next" ([Nature](#)).

Peer-Reviewed Articles

Convalescent Plasma

JAMA Oncol: [Association of Convalescent Plasma Therapy With Survival in Patients With Hematologic Cancers and COVID-19](#) (17 June 2021)

"Question Is convalescent plasma therapy associated with improved outcomes of hospitalized patients with COVID-19 and hematologic cancer?

Findings In this cohort study of 966 patients with hematologic cancer and COVID-19, after adjustment for potential confounding factors, convalescent plasma treatment was associated with a significantly improved 30-day mortality in the 143 individuals who received it. This association remained significant after propensity score matching.

Meaning These findings suggest a potential survival benefit in the administration of convalescent plasma to patients with hematologic cancers and COVID-19."

eLife: [Convalescent plasma use in the USA was inversely correlated with COVID-19 mortality](#) (04 June 2021, updated 15 June 2021)

"Background: The US Food and Drug Administration authorized COVID-19 convalescent plasma (CCP) therapy for hospitalized COVID-19 patients via the Expanded Access Program (EAP) and the Emergency Use Authorization (EUA), leading to use in about 500,000 patients during the first year of the pandemic for the USA.

Methods: We tracked the number of CCP units dispensed to hospitals by blood banking organizations and correlated that usage with hospital admission and mortality data.

Results: CCP usage per admission peaked in Fall 2020, with more than 40% of inpatients estimated to have received CCP between late September and early November 2020.

However, after randomized controlled trials failed to show a reduction in mortality, CCP usage per admission declined steadily to a nadir of less than 10% in March 2021. We found a strong inverse correlation ($r = -0.52$, $p=0.002$) between CCP usage per hospital admission and deaths occurring 2 weeks after admission, and this finding was robust to examination of deaths taking place 1, 2, or 3 weeks after admission. Changes in the number of hospital admissions, SARS-CoV-2 variants, and age of patients could not explain these findings. The retreat from CCP usage might have resulted in as many as 29,000 excess deaths from mid-November 2020 to February 2021.

Conclusions: A strong inverse correlation between CCP use and mortality per admission in the USA provides population-level evidence consistent with the notion that CCP reduces mortality in COVID-19 and suggests that the recent decline in usage could have resulted in excess deaths."

Anticoagulation

JAMA Netw Open: [Trends in Venous Thromboembolism Anticoagulation in Patients Hospitalized With COVID-19](#) (11 June 2021)

"Question What is the frequency with which patients hospitalized with COVID-19 are treated with venous thromboembolism (VTE) prophylactic- and treatment-dose anticoagulation, and what is the association of anticoagulation with in-hospital and 60-day mortality?

Findings In this cohort study of 1351 patients hospitalized with COVID-19 in which 1127 patients received anticoagulation, 34.8% missed 2 or more days of VTE prophylaxis. Use of only prophylactic-dose or treatment-dose anticoagulation was associated with lower in-hospital mortality vs no anticoagulation; however, only prophylactic-dose anticoagulation remained associated with lower mortality at 60 days.

Meaning These findings suggest that prophylactic-dose VTE anticoagulation may be optimal therapy for patients hospitalized with COVID-19."

See also: [invited commentary](#)

NEJM: [Adjunct Immune Globulin for Vaccine-Induced Thrombotic Thrombocytopenia](#) (09 June 2021)

"The use of high-dose intravenous immune globulin (IVIG) plus anticoagulation is recommended for the treatment of vaccine-induced immune thrombotic thrombocytopenia (VITT), a rare side effect of adenoviral vector vaccines against coronavirus disease 2019 (Covid-19). We describe the response to IVIG therapy in three of the first patients in whom VITT was identified in Canada after the receipt of the ChAdOx1 nCoV-19 vaccine. The patients were between the ages of 63 and 72 years; one was female. At the time of this report, Canada had restricted the use of the ChAdOx1 nCoV-19 vaccine to persons who were 55 years of age or older on the basis of reports that VITT had occurred primarily in younger persons. Two of the patients in our study presented with limb-artery thrombosis; the third had cerebral venous and arterial thrombosis. Variable patterns of serum-induced platelet activation were observed in response to heparin and platelet factor 4 (PF4), indicating the heterogeneity of the manifestations of VITT in serum. After the initiation of IVIG, reduced antibody-induced platelet activation in serum was seen in all three patients."

Combination Therapies

Clin Infect Dis: [Improved survival among hospitalized patients with COVID-19 treated with remdesivir and dexamethasone. A nationwide population-based cohort study](#) (10 June 2021)

"Background: There is limited data on outcomes of moderate to severe Coronavirus disease 2019 (COVID-19) among patients treated with remdesivir and dexamethasone in a real-world setting.

Objective: To compare the effectiveness of standard of care (SOC) alone vs SOC plus remdesivir and dexamethasone.

Methods: Two population-based nationwide cohorts of individuals hospitalized with COVID-19 during February through December 2020. Death within 30 days and need of mechanical ventilation (MV) were compared by inverse probability of treatment weighted (ITPW) logistic regression analysis and shown as odds ratio (OR) with 95% confidence interval (CI).

Results: The 30-d mortality rate of 1694 individuals treated with remdesivir and dexamethasone in addition to SOC was 12.6% compared to 19.7% for 1053 individuals receiving SOC alone. This corresponded to a weighted OR of 30-day mortality of 0.47 (95% CI, 0.38-0.57) for patients treated with remdesivir and dexamethasone compared to patients receiving SOC alone. Similarly, progression to MV was reduced (OR 0.36 (95% CI, 0.29-0.46)).

Conclusions and relevance: Treatment of moderate to severe COVID-19 during June through December that included remdesivir and dexamethasone was associated with reduced 30-day mortality and need of MV compared to treatment in February through May."

Neurologic Manifestations

J Neurol Neurosurg Psychiatry: [Neurology and neuropsychiatry of COVID-19: a systematic review and meta-analysis of the early literature reveals frequent CNS manifestations and key emerging narratives](#) (03 June 2021)

"There is accumulating evidence of the neurological and neuropsychiatric features of infection with SARS-CoV-2. In this systematic review and meta-analysis, we aimed to describe the characteristics of the early literature and estimate point prevalences for neurological and neuropsychiatric manifestations.

We searched MEDLINE, Embase, PsycINFO and CINAHL up to 18 July 2020 for randomised controlled trials, cohort studies, case-control studies, cross-sectional studies and case series. Studies reporting prevalences of neurological or neuropsychiatric symptoms were synthesised into meta-analyses to estimate pooled prevalence.

13 292 records were screened by at least two authors to identify 215 included studies, of which there were 37 cohort studies, 15 case-control studies, 80 cross-sectional studies and 83 case series from 30 countries. 147 studies were included in the meta-analysis. The symptoms with the highest prevalence were anosmia (43.1% (95% CI 35.2% to 51.3%), n=15 975, 63 studies), weakness (40.0% (95% CI 27.9% to 53.5%), n=221, 3 studies), fatigue (37.8% (95% CI 31.6% to 44.4%), n=21 101, 67 studies), dysgeusia (37.2% (95% CI 29.8% to 45.3%), n=13 686, 52 studies), myalgia (25.1% (95% CI 19.8% to 31.3%), n=66 268, 76

studies), depression (23.0% (95% CI 11.8% to 40.2%), n=43 128, 10 studies), headache (20.7% (95% CI 16.1% to 26.1%), n=64 613, 84 studies), anxiety (15.9% (5.6% to 37.7%), n=42 566, 9 studies) and altered mental status (8.2% (95% CI 4.4% to 14.8%), n=49 326, 19 studies). Heterogeneity for most clinical manifestations was high.

Neurological and neuropsychiatric symptoms of COVID-19 in the pandemic's early phase are varied and common. The neurological and psychiatric academic communities should develop systems to facilitate high-quality methodologies, including more rapid examination of the longitudinal course of neuropsychiatric complications of newly emerging diseases and their relationship to neuroimaging and inflammatory biomarkers."

BMC Infect Dis: [Central and peripheral nervous system involvement by COVID-19: a systematic review of the pathophysiology, clinical manifestations, neuropathology, neuroimaging, electrophysiology, and cerebrospinal fluid findings](#) (02 June 2021)

"Background: SARS-CoV-2 can affect the human brain and other neurological structures. An increasing number of publications report neurological manifestations in patients with COVID-19. However, no studies have comprehensively reviewed the clinical and paraclinical characteristics of the central and peripheral nervous system's involvement in these patients. This study aimed to describe the features of the central and peripheral nervous system involvement by COVID-19 in terms of pathophysiology, clinical manifestations, neuropathology, neuroimaging, electrophysiology, and cerebrospinal fluid findings.

Methods: We conducted a comprehensive systematic review of all the original studies reporting patients with neurological involvement by COVID-19, from December 2019 to June 2020, without language restriction. We excluded studies with animal subjects, studies not related to the nervous system, and opinion articles. Data analysis combined descriptive measures, frequency measures, central tendency measures, and dispersion measures for all studies reporting neurological conditions and abnormal ancillary tests in patients with confirmed COVID-19.

Results: A total of 143 observational and descriptive studies reported central and peripheral nervous system involvement by COVID-19 in 10,723 patients. Fifty-one studies described pathophysiologic mechanisms of neurological involvement by COVID-19, 119 focused on clinical manifestations, 4 described neuropathology findings, 62 described neuroimaging findings, 28 electrophysiology findings, and 60 studies reported cerebrospinal fluid results. The reviewed studies reflect a significant prevalence of the nervous system's involvement in patients with COVID-19, ranging from 22.5 to 36.4% among different studies, without mortality rates explicitly associated with neurological involvement by SARS-CoV-2. We thoroughly describe the clinical and paraclinical characteristics of neurological involvement in these patients.

Conclusions: Our evidence synthesis led to a categorical analysis of the central and peripheral neurological involvement by COVID-19 and provided a comprehensive explanation of the reported pathophysiological mechanisms by which SARS-CoV-2 infection may cause neurological impairment. International collaborative efforts and exhaustive neurological registries will enhance the translational knowledge of COVID-19's central and peripheral neurological involvement and generate therapeutic decision-making strategies."

Pre-Existing Conditions, Comorbidities, and Impact on Other Diseases

News in Brief

"How COVID-19 can lead to diabetes" ([NIH Blog](#)).

Peer-Reviewed Articles

JAMA Neurol: [Association Between SARS-CoV-2 Infection and Immune-Mediated Myopathy in Patients Who Have Died](#) (11 June 2021)

"Question Is there a COVID-19-associated myopathy, and is it a viral or postviral phenomenon?

Findings In this case-control autopsy study, 26 of 43 individuals (60%) who had died with a diagnosis of COVID-19 showed signs of muscle inflammation, ranging from mild to severe inflammatory myopathy. Inflammation was more pronounced in patients who were chronically ill and those who had seroconverted to SARS-CoV-2 than those who died after acute or subacute courses of COVID-19 and those who died of other illnesses, and no evidence was found for a direct infection of muscle tissue.

Meaning In this study, SARS-CoV-2 was associated with an immune-mediated myopathy."

JAMA Oncol: [Association of COVID-19 mRNA Vaccine With Ipsilateral Axillary Lymph Node Reactivity on Imaging](#) (10 June 2021)

"This cohort study examines ipsilateral axillary nodal reactivity seen on positron emission tomographic and computed tomographic imaging after intramuscular administration of the coronavirus 2019 mRNA vaccines."

Eur Heart J Qual Care Clin Outcomes: [Cardiovascular risk factors, cardiovascular disease, and COVID-19: an umbrella review of systematic reviews](#) (09 June 2021)

"Aims: To consolidate evidence to determine (i) the association between cardiovascular risk factors and health outcomes with coronavirus 2019 (COVID-19); and (ii) the impact of COVID-19 on cardiovascular health.

Methods and results: An umbrella review of systematic reviews was conducted. Fourteen medical databases and pre-print servers were searched from 1 January 2020 to 5 November 2020. The review focused on reviews rated as moderate or high-quality using the AMSTAR 2 tool. Eighty-four reviews were identified; 31 reviews were assessed as moderate quality and one was high-quality. The following risk factors were associated with higher mortality and severe COVID-19: renal disease [odds ratio (OR) (95% confidence interval) for mortality 3.07 (2.43-3.88)], diabetes mellitus [OR 2.09 (1.80-2.42)], hypertension [OR 2.50 (2.02-3.11)], smoking history [risk ratio (RR) 1.26 (1.20-1.32)], cerebrovascular disease [RR 2.75 (1.54-4.89)], and cardiovascular disease [OR 2.65 (1.86-3.78)]. Liver disease was associated with higher odds of mortality [OR 2.81 (1.31-6.01)], but not severe COVID-19. Current smoking was associated with a higher risk of severe COVID-19 [RR 1.80 (1.14-2.85)], but not mortality. Obesity associated with higher odds of mortality [OR 2.18 (1.10-4.34)], but there was an absence of evidence for severe COVID-19. In patients hospitalized with COVID-19, the following incident cardiovascular complications were identified: acute heart failure (2%), myocardial infarction (4%), deep vein thrombosis (7%), myocardial injury (10%), angina (10%), arrhythmias (18%), pulmonary embolism (19%), and venous thromboembolism (25%).

Conclusion: Many of the risk factors identified as associated with adverse outcomes with COVID-19 are potentially modifiable. Primary and secondary prevention strategies that target cardiovascular risk factors may improve outcomes for people following COVID-19."

Cancer: [COVID-19 outcomes in hospitalized patients with active cancer: Experiences from a major New York City health care system](#) (07 June 2021)

"Background: The authors sought to study the risk factors associated with severe outcomes in hospitalized coronavirus disease 2019 (COVID-19) patients with cancer.

Methods: The authors queried the New York University Langone Medical Center's records for hospitalized patients who were polymerase chain reaction-positive for severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) and performed chart reviews on patients with cancer diagnoses to identify patients with active cancer and patients with a history of cancer. Descriptive statistics were calculated and multivariable logistic regression was used to determine associations between clinical, demographic, and laboratory characteristics with outcomes, including death and admission to the intensive care unit.

Results: A total of 4184 hospitalized SARS CoV-2+ patients, including 233 with active cancer, were identified. Patients with active cancer were more likely to die than those with a history of cancer and those without any cancer history (34.3% vs 27.6% vs 20%,

respectively; $P < .01$). In multivariable regression among all patients, active cancer (odds ratio [OR], 1.89; CI, 1.34-2.67; $P < .01$), older age (OR, 1.06; CI, 1.05-1.06; $P < .01$), male sex (OR for female vs male, 0.70; CI, 0.58-0.84; $P < .01$), diabetes (OR, 1.26; CI, 1.04-1.53; $P = .02$), morbidly obese body mass index (OR, 1.87; CI, 1.24-2.81; $P < .01$), and elevated D-dimer (OR, 6.41 for value >2300 ; CI, 4.75-8.66; $P < .01$) were associated with increased mortality. Recent cancer-directed medical therapy was not associated with death in multivariable analysis. Among patients with active cancer, those with a hematologic malignancy had the highest mortality rate in comparison with other cancer types (47.83% vs 28.66%; $P < .01$).

Conclusions: The authors found that patients with an active cancer diagnosis were more likely to die from COVID-19. Those with hematologic malignancies were at the highest risk of death. Patients receiving cancer-directed therapy within 3 months before hospitalization had no overall increased risk of death."

Long COVID / Post-COVID Period

News in Brief

The CDC has issued interim guidance on how to evaluate and care for patients with 'post-COVID conditions' ([CDC](#)).

"As more kids go down the 'deep, dark tunnel' of long Covid, doctors still can't predict who is at risk" ([STAT](#)).

"Why are women more prone to long Covid? While men over 50 tend to suffer the most acute symptoms of coronavirus, women who get long Covid outnumber men by as much as four to one" ([Guardian](#)).

Long Reads

"Little-known illnesses turning up in covid long-haulers" ([KHN](#)).

"The four most urgent questions about long COVID: Scientists are starting to get insights into the lingering disorder that affects some people infected with SARS-CoV-2 — but many mysteries remain unsolved" ([Nature](#)).

Webinars and Calls

WHAT: CDC Clinical Outreach and Communication Activity (COCA): Evaluating and Caring for Patients with Post-COVID Conditions

WHEN: Thursday, 17 June 2021 (recorded)

DETAILS: "During this COCA Call, clinicians will learn about the Centers for Disease Control and Prevention's new interim guidance which provides a framework for healthcare providers in their initial assessment, evaluation, management, and follow-up of persons with possible post-COVID conditions. Post-COVID conditions refer to the wide range of physical and mental health consequences experienced by some patients that are present four or more weeks after SARS-CoV-2 infection, including by patients who had initial mild or asymptomatic acute infection.

Post-COVID conditions are still being characterized and include symptoms such as cognitive difficulties, fatigue, headache, dyspnea, and palpitations. Subject matter experts, physicians, and patient representatives from across the United States collaborated to develop the new guidance. Rapid recognition by healthcare providers of patients with post-COVID conditions and multidisciplinary care using the assessments and approaches described in this guidance could improve the wellbeing and treatment of people with post-COVID conditions."

Includes CE option.

MORE INFO: https://emergency.cdc.gov/coca/calls/2021/callinfo_061721.asp

Special Reports and Other Resources

FAIR Health: [A Detailed Study of Patients with Long-Haul COVID: An Analysis of Private Healthcare Claims \[pdf\]](#) (15 June 2021)

"Many patients recover from COVID-19 within a few weeks, but some exhibit persistent or new symptoms more than four weeks after first being diagnosed. Patients with such post-COVID conditions are variously referred to as having long-haul COVID, long COVID or post-acute sequelae of COVID-19 (PASC).

Using longitudinal data from a database of over 34 billion private healthcare claim records, FAIR Health studied a total of 1,959,982 COVID-19 patients for the prevalence of post-COVID conditions 30 days or more after their initial diagnosis with COVID-19. To FAIR Health's knowledge, this is the largest population of COVID-19 patients so far studied for post-COVID

conditions. The patients' post-COVID conditions were analyzed, with the most common conditions identified. Particular attention was given to age and gender, mental health conditions and death.

Among the key findings:

- Of patients who had COVID-19, 23.2 percent had at least one post-COVID condition.
- Post-COVID conditions were found to a greater extent in patients who had more severe cases of COVID-19, but also in a substantial share of patients whose cases lacked symptoms. Of patients who were hospitalized with COVID-19, the percentage that had a post-COVID condition was 50 percent; of patients who were symptomatic but not hospitalized, 27.5 percent; and of patients who were asymptomatic, 19 percent.
- The five most common post-COVID conditions across all ages, in order from most to least common, were pain, breathing difficulties, hyperlipidemia, malaise and fatigue, and hypertension.
- The ranking of the most common post-COVID conditions varied by age group. For example, in the pediatric population (0-18), pain and breathing difficulties were the top two conditions, as in the all-ages cohort, but intestinal issues, rather than hyperlipidemia, were the third most common.
- Most of the post-COVID conditions that were evaluated were associated more with females than males. In the case of 12 conditions, however, males more commonly had the condition diagnosed than females. For example, of patients who had post-COVID cardiac inflammation, 52 percent were male and 48 percent female. By age, the largest share (25.4 percent) with this condition was found in a young cohort—individuals aged 19-29.
- Of the four mental health conditions evaluated as post-COVID conditions, anxiety was associated with the highest percentage of patients after COVID-19 in all age groups. Depression was second, adjustment disorders third and tic disorders fourth.
- The odds of death 30 days or more after initial diagnosis with COVID-19 were 46 times higher for patients who were hospitalized with COVID-19 and discharged than patients who had not been hospitalized (odds ratio[OR]=46.020,95percentconfidence interval[CI], 34.778-60.897,P<0.001). Of COVID-19 patients who were hospitalized and discharged, 0.5 percent died 30 days or more after their initial diagnosis.
- Among COVID-19 patients with preexisting conditions, intellectual disabilities were associated with the highest odds of death 30 days or more after initial COVID-19 diagnosis (OR=3.082,95percentCI, 1.183-8.029,P=0.0212)."

Women's Health, Pregnancy, and Perinatal Care

Peer-Reviewed Articles

MMWR: [COVID-19 Vaccination Coverage Among Pregnant Women During Pregnancy — Eight Integrated Health Care Organizations, United States, December 14, 2020–May 8, 2021](#) (18 June 2021, early release 15 June 2021)

"What is already known about this topic? Pregnant women are at increased risk for severe illness and death from COVID-19.

What is added by this report? As of May 8, 2021, 16.3% of pregnant women identified in CDC's Vaccine Safety Datalink had received ≥ 1 dose of a COVID-19 vaccine during pregnancy in the United States. Vaccination was lowest among Hispanic (11.9%) and non-Hispanic Black women (6.0%) and women aged 18–24 years (5.5%) and highest among non-Hispanic Asian women (24.7%) and women aged 35–49 years (22.7%).

What are the implications for public health practice? Improving outreach to and engagement with health care providers and pregnant women, especially those who are younger and from racial and ethnic minority groups, could increase vaccine confidence and thus coverage of COVID-19 vaccination in this population."

Pediatric Population

News in Brief

Pfizer is expanding its vaccine clinical trials to younger children aged 5–11 years ([ABC](#)).

Moderna filed for an EUA from the FDA for its COVID-19 vaccine in adolescents ([Moderna](#)).

"Drop in childhood vaccinations during pandemic may raise risk of other outbreaks when schools reopen, CDC says" ([WP](#); see also: MMWR report below).

"Children in rural areas face increasing barriers to pediatric care, study finds" ([STAT](#); see also: Pediatrics article, below).

Peer-Reviewed Articles

JAMA Netw Open: [International Analysis of Electronic Health Records of Children and Youth Hospitalized With COVID-19 Infection in 6 Countries](#) (11 June 2021)

"Question What are international trends in hospitalizations for children and youth with SARS-CoV-2, and what are the epidemiological and clinical features of these patients?

Findings This cohort study of 671 children and youth found discrete surges in hospitalizations with variable trends and timing across countries. Common complications included cardiac arrhythmias and viral pneumonia, and laboratory findings included elevations in markers of inflammation and abnormalities of coagulation; few children and youth were treated with medications directed specifically at SARS-CoV-2.

Meaning These findings suggest large-scale informatics-based approaches used to incorporate electronic health record data across health care systems can provide an efficient source of information to monitor disease activity and define epidemiological and clinical features of pediatric patients hospitalized with SARS-CoV-2 infections."

JAMA Netw Open: [Bilateral Chilblain-like Lesions of the Toes Characterized by Microvascular Remodeling in Adolescents During the COVID-19 Pandemic](#) (10 June 2021)

"Question Are chilblain-like lesions of the toes associated with SARS-CoV-2 infection or is the association merely temporal?

Findings This case series of 17 adolescents found that chilblain-like lesions of the toes emerged during the COVID-19 pandemic in otherwise healthy adolescents without signs of SARS-CoV-2 infection or other inflammatory, autoimmune, or thrombophilic phenomena.

Meaning These results suggest that chilblain-like lesions are not associated with systemic or localized SARS-CoV-2 infection."

See also: [invited commentary](#)

JAMA Netw Open: [Incidence of Multisystem Inflammatory Syndrome in Children Among US Persons Infected With SARS-CoV-2](#) (10 June 2021)

"Question What was the incidence of multisystem inflammatory syndrome in children (MIS-C) among persons with SARS-CoV-2 infection in the US during April to June 2020?

Findings In this cohort study of 248 persons with MIS-C, MIS-C incidence was 5.1 persons per 1 000 000 person-months and 316 persons per 1 000 000 SARS-CoV-2 infections in persons younger than 21 years. Incidence was higher among Black, Hispanic or Latino, and Asian or Pacific Islander persons compared with White persons and in younger persons compared with older persons.

Meaning These findings suggest that MIS-C was a rare complication of SARS-CoV-2 infection; further study is needed to understand why MIS-C incidence varied by race/ethnicity and age group."

JAMA Netw Open: [Underlying Medical Conditions Associated With Severe COVID-19 Illness Among Children](#) (07 June 2021)

"Question Among children with a COVID-19 diagnosis, what conditions are common, and which are associated with severe COVID-19 illness?

Findings In this cross-sectional study of 43 465 patients aged 18 years or younger with COVID-19, more than one-quarter had 1 or more underlying condition; asthma, obesity, neurodevelopmental disorders, and certain mental health conditions were most common. Certain conditions as well as medical complexity were associated with a higher risk of severe COVID-19 illness.

Meaning These findings expand the knowledge available regarding children with COVID-19 and could inform pediatric clinical practice and public health priorities, such as prevention and mitigation of COVID-19."

J Infect: [Differences between children with severe acute lower respiratory infection with or without SARS-CoV-2 infection](#) (03 June 2021)

"Aim: To compare clinical features and outcome of children with severe acute lower respiratory infection (ALRI) with or without SARS-CoV-2 infection admitted to Paediatric Intensive Care Unit (PICU).

Methods: For this retrospective cohort study, all children aged<17 years admitted with severe ALRI at a PICU, in Salvador, Brazil were evaluated. Investigation of SARS-CoV-2 infection was performed by real-time reverse-transcription PCR. Clinical data, physical findings upon admission and outcome were registered. Patients were categorized by with or without SARS-CoV-2 infection. Outcomes were death and invasive mechanical ventilation (IMV).

Results: We enrolled 210 patients, whose median age was 2.8 years (IQR: 7.1 months-6.2 years). IMV was used in 33 (15.7%; 95%CI 11.3%-21.1%) patients. Eight (3.8%; 95%CI 1.8%-7.1%) cases died. 62 patients (29.5%) tested positive for SARS-CoV-2. Male gender (67.7% vs. 52.7%, P=0.045) and sickle cell disease (6.5% vs. 0%, P=0.007) were associated with SARS-CoV-2 infection. Wheezing upon admission was more common in patients without SARS-CoV-2 infection (38.5% vs. 21.0%, P=0.01). IMV was more frequent among patients with SARS-CoV-2 infection (25.8% vs. 11.5%, P=0.009) as well as death (8.1% vs. 2.0%, P=0.05).

Conclusion: Children with severe ALRI infection with SARS-CoV-2 need IMV more frequently than those without it."

Cardiology

Cardiol Young: [Cardiac manifestations and short-term outcomes of Multisystem Inflammatory Syndrome in Middle Eastern Children during the COVID-19 pandemic: A case series](#) (17 June 2021)

"We herein report on a series of 4 patients presented to our tertiary care center with features of multisystem inflammatory syndrome in children (MIS-C) and cardiac involvement. Two of our patients had recent exposure to a COVID-19 positive patient, 1 had recent documented infection, and another had no known positive contact. All patients tested positive for Severe acute respiratory syndrome coronavirus 2 Immunoglobulin G (SARS-CoV-2 IgG) antibody at the time of presentation. All of them fulfilled the diagnostic criteria according to World Health Organization Centers for Disease Control or the British guidelines for MISC (fever for ≥ 3 days, multisystem involvement (at least 2), elevated markers of inflammation and no other alternative diagnosis). (1, 2,3) Cardiac involvement was variable ranging from isolated ectasia of the coronary arteries to full blown pan-carditis: severe biventricular dysfunction, multi-valvar involvement, and pericardial effusion. All our patient received Intravenous immunoglobulin IVIG (2 g/kg), methylprednisolone, and aspirin and some required inotropic support and ICU admission. Remarkably, all our patients showed significant improvement in their cardiac disease within few days as evident on serial echocardiographic evaluation. However, we stress the need for long term follow up as one of our patients demonstrated mild LV myocardial scarring as evident by gadolinium late enhancement on a Cardiac MRI."

Pediatrics: [Symptomatic Acute Myocarditis in Seven Adolescents Following Pfizer-BioNTech COVID-19 Vaccination](#) (04 June 2021)

"Trials of coronavirus disease 2019 (COVID-19) vaccination included limited numbers of children so may not have detected rare but important adverse events in this population.

We report seven cases of acute myocarditis or myopericarditis in healthy male adolescents who presented with chest pain all within four days after the second dose of Pfizer-BioNTech COVID-19 vaccination. Five patients had fever around the time of presentation. Acute COVID-19 was ruled out in all 7 cases based on negative severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) real-time reverse transcription polymerase chain reaction (PCR) tests of specimens obtained using nasopharyngeal swabs.

None of the patients met criteria for multi-system inflammatory syndrome in children (MIS-C). Six of the 7 patients had negative SARS-CoV-2 nucleocapsid antibody assays, suggesting no prior infection. All patients had an elevated troponin. Cardiac magnetic resonance imaging (MRI) revealed late gadolinium enhancement characteristic of myocarditis. All 7 patients resolved their symptoms rapidly. Three patients were treated with non-steroidal

anti-inflammatory drugs (NSAIDs) only and 4 received intravenous immune globulin (IVIG) and corticosteroids.

This report provides a summary of each adolescent's clinical course and evaluation. No causal relationship between vaccine administration and myocarditis has been established. Continued monitoring and reporting to the Food and Drug Administration (FDA) Vaccine Adverse Event Reporting System (VAERS) is strongly recommended."

Vaccinations

Pediatrics: [Pediatric Vaccination During the COVID-19 Pandemic](#) (17 June 2021)

"OBJECTIVES The impact of the coronavirus disease 2019 pandemic on vaccination coverage, critical to preventing vaccine-preventable diseases, has not been assessed during the reopening period.

METHODS Vaccine uptake and vaccination coverage for recommended vaccines and for measles-containing vaccines at milestone ages were assessed in a large cohort of children aged 0 to 18 years in Southern California during January to August 2020 and were compared with those in the same period in 2019. Differences in vaccine uptake and vaccination coverage (recommended vaccines and measles-containing vaccines) in prepandemic (January to March), stay-at-home (April to May), and reopening (June to August) periods in 2020 and 2019 were compared.

RESULTS Total and measles-containing vaccine uptake declined markedly in all children during the pandemic period in 2020 compared with 2019, but recovered in children aged 0 to 23 months. Among children aged 2 to 18 years, measles-containing vaccine uptake recovered, but total vaccine uptake remained lower. Vaccination coverage (recommended and measles-containing vaccines) declined and remained reduced among most milestone age cohorts ≤24 months during the pandemic period, whereas recommended vaccination coverage in older children decreased during the reopening period in 2020 compared with 2019.

CONCLUSIONS Pediatric vaccine uptake decreased dramatically during the pandemic, resulting in decreased vaccination coverage that persisted or worsened among several age cohorts during the reopening period. Additional strategies, including immunization tracking, reminders, and recall for needed vaccinations, particularly during virtual visits, will be required to increase vaccine uptake and vaccination coverage and reduce the risk of outbreaks of vaccine-preventable diseases."

MMWR: [Impact of the COVID-19 Pandemic on Administration of Selected Routine Childhood and Adolescent Vaccinations — 10 U.S. Jurisdictions, March–September 2020](#) (11 June 2021)

"What is already known about this topic? Early reports during the COVID-19 pandemic documented a marked decline in pediatric vaccine ordering and administration, placing U.S. children and adolescents at risk for vaccine-preventable diseases.

What is added by this report? Analysis of immunization information systems data from 10 U.S. jurisdictions indicated a substantial decrease in administered vaccine doses during March–May 2020 compared with the same period during 2018 and 2019. Although administered doses increased during June–September 2020, this increase was not sufficient to achieve catch-up coverage.

What are the implications for public health practice? To prevent outbreaks of vaccine-preventable diseases, health care providers should assess the vaccination status of all pediatric patients, including adolescents, and contact those who are behind schedule to ensure that all children and adolescents are fully vaccinated."

Disparities

Pediatrics: [Availability of Pediatric Inpatient Services in the United States](#) (14 June 2021)

"Objectives: We sought to evaluate trends in pediatric inpatient unit capacity and access and to measure pediatric inpatient unit closures across the United States.

Methods: We performed a retrospective study of 4720 US hospitals using the 2008-2018 American Hospital Association survey. We used linear regression to describe trends in pediatric inpatient unit and PICU capacity. We compared trends in pediatric inpatient days and bed counts by state. We examined changes in access to care by calculating distance to the nearest pediatric inpatient services by census block group. We analyzed hospital characteristics associated with pediatric inpatient unit closure in a survival model.

Results: Pediatric inpatient units decreased by 19.1% (34 units per year; 95% confidence interval [CI] 31 to 37), and pediatric inpatient unit beds decreased by 11.8% (407 beds per year; 95% CI 347 to 468). PICU beds increased by 16.0% (66.9 beds per year; 95% CI 53 to 81), primarily at children's hospitals. Rural areas experienced steeper proportional declines in pediatric inpatient unit beds (-26.1% vs -10.0%). Most states experienced decreases in both pediatric inpatient unit beds (median state -18.5%) and pediatric inpatient days (median state -10.0%). Nearly one-quarter of US children experienced an increase in distance to their nearest pediatric inpatient unit. Low-volume pediatric units and those without an associated PICU were at highest risk of closing.

Conclusions: Pediatric inpatient unit capacity is decreasing in the United States. Access to inpatient care is declining for many children, particularly those in rural areas. PICU beds are

increasing, primarily at large children's hospitals. Policy and surge planning improvements may be needed to mitigate the effects of these changes."

Mental Health

Lancet Psychiatry: [Depressive symptoms, mental wellbeing, and substance use among adolescents before and during the COVID-19 pandemic in Iceland: a longitudinal, population-based study](#) (03 June 2021)

"Background: Adolescence represents a crucial developmental period in shaping mental health trajectories. In this study, we investigated the effect of the COVID-19 pandemic on mental health and substance use during this sensitive developmental stage.

Methods: In this longitudinal, population-based study, surveys were administered to a nationwide sample of 13-18-year-olds in Iceland in October or February in 2016 and 2018, and in October, 2020 (during the COVID-19 pandemic). The surveys assessed depressive symptoms with the Symptom Checklist-90, mental wellbeing with the Short Warwick Edinburgh Mental Wellbeing Scale, and the frequency of cigarette smoking, e-cigarette use, and alcohol intoxication. Demographic data were collected, which included language spoken at home although not ethnicity data. We used mixed effects models to study the effect of gender, age, and survey year on trends in mental health outcomes.

Findings: 59 701 survey responses were included; response rates ranged from 63% to 86%. An increase in depressive symptoms (β 0·57, 95% CI 0·53 to 0·60) and worsened mental wellbeing (β -0·46, 95% CI -0·49 to -0·42) were observed across all age groups during the pandemic compared with same-aged peers before COVID-19. These outcomes were significantly worse in adolescent girls compared with boys (β 4·16, 95% CI 4·05 to 4·28, and β -1·13, 95% CI -1·23 to -1·03, respectively). Cigarette smoking (OR 2·61, 95% CI 2·59 to 2·66), e-cigarette use (OR 2·61, 95% CI 2·59 to 2·64), and alcohol intoxication (OR 2·59, 95% CI 2·56 to 2·64) declined among 15-18-year-olds during COVID-19, with no similar gender differences.

Interpretation: Our results suggest that COVID-19 has significantly impaired adolescent mental health. However, the decrease observed in substance use during the pandemic might be an unintended benefit of isolation, and might serve as a protective factor against future substance use disorders and dependence. Population-level prevention efforts, especially for girls, are warranted."

Impact on Healthcare Workers

Peer-Reviewed Articles

JAMA Netw Open: [International Medical Graduate Physician Deaths From COVID-19 in the United States](#) (11 June 2021)

"This case series study examines mortality rates due to COVID-19 among all physicians and international medical graduate physicians in the US."

JAMA Netw Open: [Secondary Use of COVID-19 Symptom Incidence Among Hospital Employees as an Example of Syndromic Surveillance of Hospital Admissions Within 7 Days](#) (17 June 2021)

"Question Can secondary use of employee symptom attestation data be used as syndromic surveillance to estimate COVID-19 hospitalizations in the communities where the employees live?"

Findings In this cohort study of 6481 hospital employees, an increased frequency of COVID-19 symptoms reported by all employees at a single hospital was associated with increased hospitalizations across 10 hospitals 7 days later.

Meaning These findings suggest that in a novel pandemic before reliable testing is available, use of nontraditional secondary data sources can be used to estimate hospital demand."

Vaccines

Clin Infect Dis: [Post-vaccination SARS-CoV-2 infections and incidence of presumptive B.1.427/B.1.429 variant among healthcare personnel at a northern California academic medical center](#) (17 June 2021)

"Background: Although mRNA-based SARS-CoV-2 vaccines report ≥90% efficacy, breakthrough infections occur. Little is known about the effectiveness of these vaccines against SARS-CoV-2 variants, including the highly-prevalent B.1.427/B.1.429 variant in California..

Methods: In this quality improvement project, we collected demographic and clinical information from post-vaccine SARS-CoV-2 cases (PVSCs), defined as health care personnel (HCP) with positive SARS-CoV-2 NAAT after receiving ≥1 vaccine dose. Available specimens were tested for L452R, N501Y and E484K mutations by RT-PCR. Mutation prevalence was compared among unvaccinated, early post-vaccinated (<=14 days after dose 1), partially vaccinated (positive test >14 days after dose 1 and ≤14 days after dose 2) and fully vaccinated (>14 days after dose 2) PVSCs.

Results: From December 2020-April 2021, >=23,090 HCPS received at least 1 dose of an mRNA-based SARS-CoV-2 vaccine, and 660 HCP cases of SARS-CoV-2 occurred of which 189 were PVSCs. Among the PVSCs, 114 (60.3%), 49 (25.9%) and 26 (13.8%) were early post-vaccination, partially vaccinated, and fully vaccinated, respectively. Of 261 available samples from vaccinated and unvaccinated HCP, 103 (39.5%), including 42 PVSCs (36.5%), had L452R mutation presumed to be B.1.427/B.1.429,. When adjusted for community prevalence of B.1.427/B.1.429, PVSCs did not have significantly elevated risk for infection with B.1.427/B.1.429 compared with unvaccinated HCP.

Conclusions: Most PVSCs occurred prior to expected onset of full, vaccine-derived immunity. Presumptive B.1.427/B.1.429 was not more prevalent in post-vaccine cases than in unvaccinated SARS-CoV-2 HCP. Continued infection control measures, particularly ≤14 days post-vaccination, and continued variant surveillance in PVSCs is imperative to control future SARS-CoV-2 surges."

JAMA Netw Open: [Incidence of SARS-CoV-2 Infection in Health Care Workers After a Single Dose of mRNA-1273 Vaccine](#) (16 June 2021)

"This study demonstrated an association between receipt of mRNA-1273 vaccine and a reduction in SARS-CoV-2 infection in HCWs beginning 8 days after dose 1. These real-world findings reflect vaccination solely with mRNA-1273 and are consistent with aggregated data for BNT162b2 and mRNA-1273 in HCWs. The first-dose risk reduction of 95% after day 14 highlights the potential for vaccination with mRNA-1273 to rapidly mitigate surges of vaccine-sensitive SARS-CoV-2 infection in HCWs."

Mental Health

JAMA Netw Open: [Academic Medicine Faculty Perceptions of Work-Life Balance Before and Since the COVID-19 Pandemic](#) (15 June 2021)

Question How is the COVID-19 pandemic associated with academic medicine faculty perceptions of work-life integration?

Findings In this survey of 1186 medical, graduate, and health professional school faculty, more faculty considered leaving since the COVID-19 pandemic than before. Faculty with children, particularly female faculty with children, were more likely to consider leaving since the pandemic.

Meaning These findings suggest that the stressors of integrating work and life are higher in female faculty than male faculty, highest in women with children, and may have been heightened by the COVID-19 pandemic."

Disaster Med Public Health Prep: [Factors Related to Self-Reported Distress Experienced by Physicians During Their First COVID-19 Triage Decisions](#) (07 June 2021)

"Objective: To identify factors associated with distress experienced by physicians during their first COVID-19 triage decisions.

Results: Of the 164 physicians studied, 20.7% experienced severe distress during their first COVID-19 triage decisions. The mean distress score was not significantly different between physicians who received just-in-time training and those who did not (6.0 ± 2.7 vs 6.2 ± 2.8 , $P=0.550$) and between physicians who received clinical guidelines and those who did not (6.0 ± 2.9 vs 6.2 ± 2.7 , $P=0.820$). Substantially increased odds of severe distress were found in physicians who reported that their first COVID-19 triage decisions were inconsistent with their core values (adjusted odds ratio 6.33, 95% confidence interval 2.03-19.76) and who reported having insufficient skills and expertise (adjusted odds ratio 2.99, 95% confidence interval 0.91-9.87).

Conclusion: About 1 in 5 physicians in New York experienced severe distress during their first COVID-19 triage decisions. Physicians with insufficient skills and expertise, and core values misaligned to triage decisions are at heightened risk of severe distress. Just-in-time training and clinical guidelines do not appear to alleviate distress experienced by physicians during their first COVID-19 triage decisions."

Mental Health, Psychosocial Issues, and Wellness

News in Brief

"10 replaceable thoughts (and 15 books) to help you survive burnout" ([KevinMD](#)).

Long read: "The 'grief pandemic' will torment Americans for years" ([KHN](#)).

Take a Break, Maybe Cool Off a Bit

If you need a dog fix, check out these photos from the 2021 Westminster Dog Show ([Atlantic](#)).

8. A chow chow cools off in the judging area on June 12, 2021. Timothy A. Clary / AFP / Getty; used without permission.

HE'S SO FLUFFY.



Special Reports and Other Resources

ASPR TRACIE: [The Experience of Chaplains During COVID-19 \[pdf\]](#) (June 2021)

"While the COVID-19 pandemic confronted professional Chaplains with distressing realities that sometimes pushed us beyond the limits of our training and ability to cope, it also highlighted our unique contributions in providing end of life care, supporting staff, and enhancing an organization's capacity to mitigate the impact of trauma and health inequities. In my own experience as the leader of Spiritual Care at Hennepin Healthcare, a Level One Trauma Center, safety net hospital in downtown Minneapolis, the pandemic presented our Chaplain team with three distinct challenges and opportunities."

Includes links to related resources on burnout, moral injury, and trauma-informed care.

ASPR TRACIE: [Topic Collection: COVID-19 Behavioral Health Resources](#) (accessed 18 June 2021)

Includes sections on general resources, managing conflict or violence, resources for responders, self-care and resilience in healthcare workers, and telehealth resources.

Peer-Reviewed Articles

MMWR: [Mental Health Among Parents of Children Aged <18 Years and Unpaid Caregivers of Adults During the COVID-19 Pandemic — United States, December 2020 and February–March 2021](#) (18 June 2021)

"What is already known about this topic? Parents of children aged <18 years and unpaid caregivers of adults have had mental health challenges before and during the COVID-19 pandemic.

What is added by this report? Among 10,444 U.S. adults surveyed during December 6–27, 2020, and February 16–March 8, 2021, parents, unpaid caregivers of adults, and parents-caregivers (persons in both roles) had significantly worse mental health than adults not in these roles, including five times the odds of any adverse mental health symptoms (parents-caregivers). Persons who had someone to rely on for support had lower odds of experiencing any adverse mental health symptoms.

What are the implications for public health practice? Parents and unpaid caregivers of adults, and particularly those in both roles, might benefit from mental health support and services tailored to their roles."

Psychol Med: [Mental Health Impact of the COVID-19 Pandemic in U.S. Military Veterans: A Population-Based, Prospective Cohort Study](#) (14 June 2021)

"Background: The coronavirus disease-2019(COVID-19) pandemic has caused myriad health, social, and economic stressors. To date, however, no known study has examined changes in mental health during the pandemic in the U.S. military veteran population.

Methods: Data were analyzed from the 2019-2020 National Health and Resilience in Veterans Study, a nationally representative, prospective cohort survey of 3,078 veterans. Pre-to-peri-pandemic changes in psychiatric symptoms were evaluated, as well as pre-pandemic risk and protective factors and pandemic-related correlates of increased psychiatric distress.

Results: The prevalence of generalized anxiety disorder (GAD) positive screens increased from pre-to peri-pandemic(7.1% to 9.4%; p<0.001)and was driven by an increase among veterans aged 45-64 years (8.2% to13.5%; p<0.001),but the prevalence of major depressive disorder and posttraumatic stress disorder positive screens remained stable. Using a continuous measure of psychiatric distress, an estimated13.2%of veterans reported a clinically meaningful pre-to-peri-pandemic increase in distress (mean=1.1 standard deviation). Veterans with a larger pre-pandemic social network size and secure attachment style were less likely to experience increased distress, whereas veterans reporting more pre-pandemic loneliness were more likely to experience increased distress. Concerns about pandemic-related social losses, mental health COVID-19 effects, and housing stability during the pandemic were associated with increased distress, over-and-above pre-pandemic factors.

Conclusions: Although most U.S. veterans showed resilience to mental health problems nearly one year into the pandemic, the prevalence of GAD positive screens increased, particularly among middle-aged veterans, and 1-of-7 veterans experienced increased distress. Clinical implications of these findings are discussed."

JAMA Netw Open: [Factors Associated With Self-reported Symptoms of Depression Among Adults With and Without a Previous COVID-19 Diagnosis](#) (11 June 2021)

"This survey study compares features of self-reported symptoms of major depression in adults with or without a prior COVID-19 diagnosis....

In this survey study, the magnitude of depressive symptoms and sociodemographic variables differed between individuals with and without prior COVID-19 illness. These differences in phenomenology and risk factors both indirectly suggest that apparent major depressive episodes following COVID-19 illness may be distinct from those typically observed in adults. Furthermore, the risk for depressive symptoms increased with greater postacute interval, rather than the gradual reduction anticipated if depressive symptoms are a consequence of acute increase in illness-associated stressors."

MMWR: [Emergency Department Visits for Suspected Suicide Attempts Among Persons Aged 12–25 Years Before and During the COVID-19 Pandemic — United States, January 2019–May 2021](#) (11 June 2021)

"What is already known about this topic? During 2020, the proportion of mental health-related emergency department (ED) visits among adolescents aged 12–17 years increased 31% compared with that during 2019.

What is added by this report? In May 2020, during the COVID-19 pandemic, ED visits for suspected suicide attempts began to increase among adolescents aged 12–17 years, especially girls. During February 21–March 20, 2021, suspected suicide attempt ED visits were 50.6% higher among girls aged 12–17 years than during the same period in 2019; among boys aged 12–17 years, suspected suicide attempt ED visits increased 3.7%.

What are the implications for public health practice? Suicide prevention requires a comprehensive approach that is adapted during times of infrastructure disruption, involves multisectoral partnerships and implements evidence-based strategies to address the range of factors influencing suicide risk."

JAMA: [Responding to Intimate Partner Violence During Telehealth Clinical Encounters](#) (08 June 2021)

"This JAMA Insights Clinical Update discusses the surge in intimate partner violence (IPV) during the COVID-19 lockdown and provides safe and patient-centered methods for primary care clinicians to screen for IPV and counsel patients during telehealth consultations."

Disparities and Health Equity

News in Brief

"Opinion: Huge disparities in vaccination rates are creating islands of vulnerability across the country" ([WP](#)).

The June supplement for *Health Security* is on systemic racism during the pandemic ([Health Security](#)).

Peer-Reviewed Articles

JAMA Netw Open: [Patient and Hospital Factors Associated With Differences in Mortality Rates Among Black and White US Medicare Beneficiaries Hospitalized With COVID-19 Infection](#) (17 June 2021)

"Question Do Black patients hospitalized with COVID-19 have worse outcomes than White patients and, if so, what is the association between worse outcomes and comorbidities vs the hospitals to which they are admitted?

Findings In this cohort study of 44 217 adult Medicare beneficiaries admitted with COVID-19 to 1188 US hospitals, odds of 30-day inpatient mortality or discharge to hospice were 11% higher for Black patients than for White patients after adjustment for patient sociodemographic and clinical characteristics. That difference was largely eliminated when adjustment was made for the hospital where care was received.

Meaning This study's findings suggest that the increased mortality among Black patients hospitalized with COVID-19 is associated with the hospitals at which Black patients disproportionately received care."

See also: [invited commentary](#)

JAMA Netw Open: [Association of Social and Behavioral Risk Factors With Mortality Among US Veterans With COVID-19](#) (09 June 2021)

"Question Are social and behavioral risk factors associated with mortality in US veterans with COVID-19?

Findings In this cohort study of 27 640 veterans who received a positive test result for COVID-19, risk factors such as housing problems, financial hardship, alcohol use, tobacco use, and substance use were not associated with higher mortality.

Meaning This study found no association between social and behavioral risk factors and death from COVID-19 in an integrated VA health system; such a system is known to transcend social vulnerabilities and has the potential to be a model of support services for households and at-risk populations in the US."

Disaster Med Public Health Prep: [Concepts and Terms for Addressing Disparities in Public Health Emergencies: Accounting for the COVID-19 Pandemic and the Social Determinants of Health in the United States](#) (08 June 2021)

"Public health emergencies, including the coronavirus (COVID-19) pandemic, highlight disproportionate impacts faced by populations with existing disparities. Concepts and terms used to describe populations disproportionately impacted in emergencies vary over time and across disciplines, but United States (U.S.) federal guidance and law require equal access to our nation's emergency resources. At all levels of emergency planning, public health and their partners must be accountable to populations with existing inequities, which requires a conceptual shift towards using the data-driven social determinants of health (SDOH). SDOH are conditions in which people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality of life

outcomes and risks. This article reviews the historic use of concepts and terms to describe populations disproportionately impacted by emergencies. It also recommends a shift in emergency activities towards interventions that target the SDOH to adequately address long-standing systemic health disparities and socioeconomic inequities in the U.S."

JAMA Netw Open: [Associations of Race/Ethnicity and Food Insecurity With COVID-19 Infection Rates Across US Counties](#) (08 June 2021)

"Question Are racial/ethnic population composition and food insecurity associated with COVID-19 infection rates?

Findings This cross-sectional study of 3133 US counties found that there was an association between race/ethnicity and COVID-19 infection rate, with an interaction with food insecurity in counties with large Black and American Indian or Alaska Native populations but not in counties with large Hispanic populations.

Meaning These findings suggest that public policy aimed at fighting COVID-19 should consider county-level food insecurity to better understand the social dynamics of the disease."

Risk, Transmission, Exposure, and Serosurveillance

News in Brief

SARS-CoV-2 was likely circulating in the US as early as December 2019, according to new research from an NIH study ([CNN](#); see also: Clin Infect Dis article on All of Us, below).

Ventilation Matters

The FDA warns that alcohol-based hand sanitizers should be applied in well ventilated areas ([FDA](#)).

Royal Caribbean delayed a cruise after 8 crew tested positive for SARS-CoV-2; previously another RC cruise had 2 guests test positive while at sea ([NBC](#); [Reuters](#)).

The [COVID-19 Aerosol timeline](#) includes studies and events documenting airborne risk of the coronavirus, along with information on other airborne diseases; see also the airborne transmission peer-reviewed articles below.

Long Reads

"Sewage sleuths helped an Arizona town beat back Covid-19. For wastewater epidemiology, that's just the start" ([STAT](#); see also: [COVIDpoops19 dashboard](#) for wastewater monitoring).

"We investigated whether digital contact tracing actually worked in the US: A year ago, engineers built apps to track potential virus exposure. Our research shows the impact has been mixed—but there's still potential" ([MIT Tech Rev](#)).

Peer-Reviewed Articles

Clin Infect Dis: [Antibodies to SARS-CoV-2 in All of Us Research Program Participants, January 2-March 18, 2020](#) (15 June 2021)

"Background: With limited SARS-CoV-2 testing capacity in the US at the start of the epidemic (January – March), testing was focused on symptomatic patients with a travel history throughout February, obscuring the picture of SARS-CoV-2 seeding and community transmission. We sought to identify individuals with SARS-CoV-2 antibodies in the early weeks of the US epidemic.

Methods: All of Us study participants in all 50 US states provided blood specimens during study visits from January 2 to March 18, 2020. A participant was considered seropositive if they tested positive for SARS-CoV-2 immunoglobulin G (IgG) antibodies on the Abbott Architect SARS-CoV-2 IgG ELISA and the EUROIMMUN SARS-CoV-2 ELISA in a sequential testing algorithm. Sensitivity and specificity of the Abbott and EUROIMMUNE ELISAs and the net sensitivity and specificity of the sequential testing algorithm were estimated with 95% confidence intervals.

Results: The estimated sensitivity of Abbott and EUROIMMUN was 100% (107/107 [96.6%, 100%]) and 90.7% (97/107 [83.5%, 95.4%]), respectively. The estimated specificity of Abbott and EUROIMMUN was 99.5% (995/1,000 [98.8%, 99.8%]) and 99.7% (997/1,000 [99.1%, 99.9%]), respectively. The net sensitivity and specificity of our sequential testing algorithm was 90.7% (97/107 [83.5%, 95.4%]) and 100.0% (1,000/1,000 [99.6%, 100%]), respectively. Of the 24,079 study participants with blood specimens from January 2 to March 18, 2020, 9 were seropositive, 7 of whom were seropositive prior to the first confirmed case in the states of Illinois, Massachusetts, Wisconsin, Pennsylvania, and Mississippi.

Conclusions: Our findings indicate SARS-CoV-2 infections weeks prior to the first recognized cases in 5 US states."

Clin Infect Dis: [Use of U.S. Blood Donors for National Serosurveillance of SARS-CoV-2 Antibodies: Basis for an Expanded National Donor Serosurveillance Program](#) (10 June 2021)

"Introduction: The REDS-IV-P Epidemiology, Surveillance and Preparedness of the Novel SARS-CoV-2 Epidemic (RESPONSE) seroprevalence study conducted monthly cross-sectional testing for SARS-CoV-2 antibodies on blood donors in six U.S. metropolitan regions to estimate the extent of SARS-COV-2 infections over time.

Study design/methods: During March-August 2020, approximately $\geq 1,000$ serum specimens were collected monthly from each region and tested for SARS-CoV-2 antibodies using a well-validated algorithm. Regional seroprevalence estimates were weighted based on demographic differences with the general population. Seroprevalence was compared with reported COVID-19 case rates over time.

Results/findings: For all regions, seroprevalence was $<1.0\%$ in March 2020. New York experienced the biggest increase (peak seroprevalence, 15.8 % in May). All other regions experienced modest increases in seroprevalence(1-2% in May-June to 2-4% in July-August). Seroprevalence was higher in younger, non-Hispanic Black, and Hispanic donors. Temporal increases in donor seroprevalence correlated with reported case rates in each region. In August, 1.3-5.6 estimated cumulative infections (based on seroprevalence data) per COVID-19 case reported to CDC.

Conclusion: Increases in seroprevalence were found in all regions, with the largest increase in New York. Seroprevalence was higher in non-Hispanic Black and Hispanic blood donors than in non-Hispanic White blood donors. SARS-CoV-2 antibody testing of blood donor samples can be used to estimate the seroprevalence in the general population by region and demographic group. The methods derived from the RESPONSE seroprevalence study served as the basis for expanding SARS-CoV-2 seroprevalence surveillance to all 50 states and Puerto Rico."

Clin Infect Dis: [The risk of symptomatic infection during a second COVID-19 wave, in SARS-CoV-2 seropositive individuals](#) (16 June 2021)

"We analyzed 221 COVID-19 cases identified between June 2020 and January 2021 in 6,074 individuals screened for IgG antibodies in May 2020, representing 77% of residents of five Italian municipalities. The adjusted relative risk of developing symptomatic infection in SARS-COV-2 seropositive participants was 0.055 (95%CI: 0.014 - 0.220)"

Disaster Med Public Health Prep: [The promise of disease detection dogs in pandemic response: lessons learned from COVID-19](#) (08 June 2021)

"One of the lessons learned from the COVID-19 pandemic is the utility of an early, flexible and rapidly deployable disease screening and detection response. The largely uncontrolled spread of the pandemic in the United States exposed a range of planning and implementation shortcomings, which if they had been in place before the pandemic emerged, may have changed the trajectory. Disease screening by detection dogs show great

promise as a non-invasive, efficient, and cost-effective screening method for COVID-19 infection. We explore evidence of their use in infectious and chronic diseases, the training, oversight, resources required for implementation, and potential uses in various settings. Disease detection dogs may contribute to the current and future public health pandemics; however, further research is needed to extend our knowledge and measurement of their effectiveness and feasibility as a public health intervention tool and efforts are needed to ensure public and political support."

Airborne Transmission

J Infect: [Evidence for lack of transmission by close contact and surface touch in a restaurant outbreak of COVID-19](#) (29 May 2021)

"Background: Coronavirus disease 2019 (COVID-19) is primarily a respiratory disease that has become a global pandemic. Close contact plays an important role in infection spread, while fomite may also be a possible transmission route. Research during the COVID-19 pandemic has identified long-range airborne transmission as one of the important transmission routes although lack solid evidence.

Methods: We examined video data related to a restaurant associated COVID-19 outbreak in Guangzhou. We observed more than 40,000 surface touches and 13,000 episodes of close contacts in the restaurant during the entire lunch duration. These data allowed us to analyse infection risk via both the fomite and close contact routes.

Results: There is no significant correlation between the infection risk via both fomite and close contact routes among those who were not family members of the index case. We can thus rule out virus transmission via fomite contact and interpersonal close contact routes in the Guangzhou restaurant outbreak. The absence of a fomite route agrees with the COVID-19 literature.

Conclusions: These results provide indirect evidence for the long-range airborne route dominating SARS-CoV-2 transmission in the restaurant. We note that the restaurant was poorly ventilated, allowing for increasing airborne SARS-CoV-2 concentration."

Build Environ: [Probable airborne transmission of SARS-CoV-2 in a poorly ventilated restaurant](#) (online 31 March 2021)

"Although airborne transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been recognized, the condition of ventilation for its occurrence is still being debated. We analyzed a coronavirus disease 2019 (COVID-19) outbreak involving three families in a restaurant in Guangzhou, China, assessed the possibility of airborne transmission, and characterized the associated environmental conditions. We collected

epidemiological data, obtained a full video recording and seating records from the restaurant, and measured the dispersion of a warm tracer gas as a surrogate for exhaled droplets from the index case. Computer simulations were performed to simulate the spread of fine exhaled droplets. We compared the in-room location of subsequently infected cases and spread of the simulated virus-laden aerosol tracer. The ventilation rate was measured using the tracer gas concentration decay method. This outbreak involved ten infected persons in three families (A, B, C). All ten persons ate lunch at three neighboring tables at the same restaurant on January 24, 2020. None of the restaurant staff or the 68 patrons at the other 15 tables became infected. During this occasion, the measured ventilation rate was 0.9 L/s per person. No close contact or fomite contact was identified, aside from back-to-back sitting in some cases. Analysis of the airflow dynamics indicates that the infection distribution is consistent with a spread pattern representative of long-range transmission of exhaled virus-laden aerosols. Airborne transmission of the SARS-CoV-2 virus is possible in crowded space with a ventilation rate of 1 L/s per person."

Indoor Air: [Droplet fate in indoor environments, or can we prevent the spread of infection?](#) (09 June 2006)

"When considering how people are infected and what can be done to prevent the infections, answers from many disciplines are sought: microbiology, epidemiology, medicine, engineering, and physics. There are many pathways to infection spread, and among the most significant from the epidemiological point of view is airborne transport. Microorganisms can become airborne when droplets are generated during speech, coughing, sneezing, vomiting, or atomization of feces during sewage removal. The fate of the droplets is governed by the physical principles of transport, with droplet size being the most important factor affecting their dispersion, deposition on surfaces and determining the survival of microorganisms within the droplets. In addition, physical characteristics of the indoor environment as well as the design and operation of building ventilation systems are of critical importance. Do we understand the mechanisms of infection spread and can we quantify the droplet dynamics under various indoor conditions? Unfortunately no, as this aspect of infection spread has attracted surprisingly little scientific interest. However, investigations of numerous cases in which a large number of people were infected show how critical the physics of microorganism spread can be. This paper reviews the state of knowledge regarding mechanisms of droplet spread and solutions available to minimize the spread and prevent infections.

Practical implications: Every day tens of millions of people worldwide suffer from viral infections of different severity at immense economic cost. There is, however, only minimal understanding of the dynamics of virus-laden aerosols, and so the ability to control and prevent virus spread is severely reduced, as was clearly demonstrated during the recent severe acute respiratory syndrome epidemic. This paper proposes the direction to

significantly advance fundamental and applied knowledge of the pathways of viral infection spread in indoor atmospheric systems, through a comprehensive multidisciplinary approach and application of state-of-the-art scientific methods. Knowledge gained will have the potential to bring unprecedented economical gains worldwide by minimizing/reducing the spread of disease."

Breakthrough Infections, Reinfections, and Coinfections

Peer-Reviewed Articles

Clin Infect Dis: [The SARS-CoV-2 mRNA vaccine breakthrough infection phenotype includes significant symptoms, live virus shedding, and viral genetic diversity](#) (12 June 2021)

"Little is known about SARS-CoV-2 'vaccine-breakthrough' infections (VBI). Here we characterize 24 VBI in predominantly young healthy persons. While none required hospitalization, a proportion endorsed severe symptoms and shed live virus as high as 4.13×10^3 PFU/mL. Infecting genotypes included both variant-of-concern (VOC) and non-VOC strains."

Emerg Infect Dis: [Multicenter Epidemiologic Study of Coronavirus Disease–Associated Mucormycosis, India](#) (04 June 2021)

"During September–December 2020, we conducted a multicenter retrospective study across India to compare epidemiology and outcomes among cases of coronavirus disease (COVID-19)–associated mucormycosis (CAM). Among 287 mucormycosis patients, 187 (65.2%) had CAM; CAM prevalence was 0.27% among hospitalized COVID-19 patients. We noted a 2.1-fold rise in mucormycosis during the study period compared with September–December 2019. Uncontrolled diabetes mellitus was the most common underlying disease among CAM and non-CAM patients. COVID-19 was the only underlying disease in 32.6% of CAM patients. COVID-19–related hypoxemia and improper glucocorticoid use independently were associated with CAM. The mucormycosis case-fatality rate at 12 weeks was 45.7% but was similar for CAM and non-CAM patients. Age, rhino-orbital-cerebral involvement, and intensive care unit admission were associated with increased mortality rates; sequential antifungal drug treatment improved mucormycosis survival. The COVID-19 pandemic has led to increases in mucormycosis in India, partly from inappropriate glucocorticoid use."

Other Infectious Diseases

News in Brief

"This man spent last year flushing hundreds of toilets. The new fear as the pandemic wanes: Legionnaires' disease" ([USA Today](#)).

The CDC issued a health advisory for interseasonal RSV in the southern US ([CDC](#)).

"A pivotal mosquito experiment could not have gone better: An extremely common microbe can stop the insects from spreading the virus that causes dengue fever" ([Atlantic](#); see also: [NEJM article of study](#) and why it matters: [NEJM letter to the editor on fatal dengue in Florida](#)).

For the sixth year in a row, sexually transmitted diseases have hit an all-time high; Virginia ranks 20th for chlamydia and 30th for gonorrhea and syphilis ([USA Today](#); see also: [CDC data \[pdf\]](#)).

The FDA has approved a drug – brincidofovir – to treat smallpox ([FDA](#)).

The US has banned importing of dogs – something that increased due to a rise in demand to adopt pets during the pandemic – from over 100 countries because of false rabies records ([NPR](#)).

Polio

The Global Polio Eradication Initiative (GPEI) is launching a new strategy that incorporates efforts to mitigate setbacks from the pandemic ([WHO](#)).

Long read: "Polio was eliminated in the Asia-Pacific. Then it suddenly came back" ([ABC Radio National](#)).

Peer-Reviewed Articles

Clin Infect Dis: [Reporting of Infectious Diseases in the United States During the COVID-19 Pandemic](#) (07 June 2021)

"Reporting of infectious diseases other than COVID-19 has been greatly decreased throughout the COVID-19 pandemic. We find this decrease varies by routes of transmission, reporting state, and COVID-19 incidence at the time of reporting. These results underscore the need for continual investment in routine surveillance efforts despite pandemic conditions."

Ethics Med Public Health: [Ethical issues in genetics and infectious diseases research: An interdisciplinary expert review](#) (07 June 2021)

"Background: Research in genetics and infectious diseases (ID) presents novel configurations of ethical, legal, and social issues (ELSIs) related to the intersection of genetics with public health regulations and the control of transmissible diseases. Such research includes work both in pathogen genetics and on the ways that human genetics affect responses to ID. This paper identifies and systematizes the unique issues at this intersection, based on an interdisciplinary expert review.

Methodology: This paper presents results of a formal issue-spotting exercise among twenty experts in public health, law and genomics, biobanking, genetic epidemiology, ID medicine and public health, philosophy, ethics and ID, ethics and genomics, and law and ID. The focus of the exercise was on the collection, storage, and sharing of genetic information relating to ID.

Results: The issue-spotting exercise highlighted the following ELSIs: risks in reporting to government authorities, return of individual research results, and resource allocation – each taking on specific configurations based on the balance between public health and individual privacy/protection.

Conclusions: The public health implications of interactions between genomics and ID frame considerations for equity and justice. In the context of the COVID-19 pandemic, these issues are especially pressing."

Statistics

Global

18 JUN 2021: 177,509,164 confirmed cases and 3,843,926 deaths

United States		top 5 states by cases					
	TOTAL US	CA	TX	FL	NY	IL	
Cases	33,509,772	3,806,154	2,982,654	2,344,321	2,110,756	1,388,515	
Deaths	600,935	63,256	52,040	37,265	53,589	25,552	

[JHU CSSE](#) as of 1000 EDT 18 June 2021

Virginia	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	678,506	21,194	10,703	14,297	17,990	9,174	8,000	36,306
Hospitalizations	30,291	1,028	426	497	1,033	684	460	1,703
Deaths	11,342	305	181	237	267	202	191	413

[VA DOH](#) as of 1000 EDT 18 June 2021